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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/601,875	10/12/00	TANGA	M TANGA2

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EXAMINER	
WILDER, C	
ART UNIT	**PAPER NUMBER**
1655	10

DATE MAILED: 06/07/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/601,875	TANGA et al.
Examiner	**Art Unit**
CB Wilder	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 28, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-25* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

1. Applicant's amendments filed March 20, 2001 and March 28, 2001 in Paper Nos. 8 and 9 are acknowledged. Claims 1, 3-5, 12-15 have been amended. Claims 17-20 have been canceled. Claims 22-25 have been added. Claims 1-16 and 21-25 are pending. The arguments have been thoroughly reviewed but are deemed moot in view of the new grounds of Rejections.

Any rejection not reiterated in this action have been withdrawn as being obviated by the amendment of the claims.

2. The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office Action.

Previous Objections and Rejections

3. The objection to the title is withdrawn in view of Applicant's amendment of the title. The claim rejection under 35 U.S.C. 112 second paragraph directed to claims 1-10, 12, and 17-20 is withdrawn in view of Applicant's amendment of the claims. The prior art rejection under are withdrawn in view of the new grounds of rejections

New grounds of Rejection

Specification

4. A substitute specification in proper idiomatic English and in compliance with 37 CFR 1.52(a) and (b) is required. The substitute specification filed must be accompanied by a statement that it contains no new matter. A substituted specification is required because of the following informalities:

(a) Numerous examples of nonidiomatic English throughout the specification, such as e.g., "untying hydrogen bonds", "substrates is", "medical care and sergeant", etc.

(b) At page 17, second paragraph "chloride arrangement is relatively supplement with respect to the oligo nucleic acid may be immobilized so as to utilize as a DNA library chip" is confusing and doesn't relate to anything known in molecular biology art.

(c) At page 19, second paragraph, "limit enxyme portion...." is confusing and doesn't relate to any known practice in molecular biology.

(d) At page 19, third paragraph, "after cutting the limit enzyme..." is confusing and doesn't relate to known practice in molecular biology.

(e) "Terminal end..." as discussed in the Examples is confusing and it is unclear what is encompassed or what is meant by the "terminal ends".

(f) Numerous spelling errors throughout the specification, such as e.g. "temperature-sensitive polymerize", "flagment", "olegonucleotide", "colled at low temperature", etc.

(h) At page 5 and throughout the specification, several abbreviations are disclosed that are not identified by the full name and it cannot be determined what is encompassed by the abbreviations.

Claim Rejections - 35 USC § 112 First Paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-16 and 22-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use solid state substrate having substantial thermal conductivity wherein the substrate has a thermal conductivity ratio equal to or more than 0.1 W/cm.K or equal to or more than 0.5 W/cm.K. There are many factors to be considered in determining whether undue experimentation is require. These factors include the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims and the quantity of experimentation which would be required in order to practice the invention as claimed. In this case, the instant invention is broadly drawn to a solid state substrate for DNA immobilization, said solid state substrate having substantial thermal conductivity for amplifying and immobilizing DNA. The specification at page 4 describes the solid state substrate and discloses wherein a thermal conductivity ratio of the substrate is obtained such that the thermal conductivity ratio is equal to or more than 0.1W/cm.K or equal to or more than 0.5 W/cm.K. The specification however fails to describes or discloses how the thermal conductivity ratio for the claimed substrate was obtained or under what conditions the thermal conductivity of the substrate was measured. No direction or

guidance is given in the Example which would enable one of skill in the art to make or use the claim substrate having a "substantial" thermal conductivity. In fact, there is no disclosure that the cited thermal conductivity ratio is indicative of a substrate with "substantial" or "excellent" thermal characteristics. As to the level of unpredictability in the art, it is well known in the art that the measurements of thermal conductivity of a substrate is highly dependent on the measurement conditions. These conditions include temperature and atmosphere pressure (e.g., air, nitrogen, vacuum) which are not disclosed or described anywhere in the specification in relation to the substrate and its thermal conductivity properties. Not only are those conditions important, but Herb et al. (5, 270,114) further teach that other factors such as lattice inhomogeneities and phonon scattering due to isotopic effect can strongly limit the thermal conductivity of a substrate by limiting heat conduction (col. 2, lines 22- col. 3, line 27). Therefore, it is unpredictable as to the thermal conductivity of the claimed substrate without knowledge of the conditions by which the measurements were obtained. In view of the foregoing undue experimentation would be required to make and use a solid state substrate having the thermal conductivity properties as disclosed in the specification.

Claim Rejections - 35 USC § 112 Second Paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his invention.

8. Claims 1-16 and 21-25 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

(a) The claims 1-16 and 21-25 are indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical, idiomatic errors and spelling errors.

(b) Claims 1-10 are indefinite at "substantial" because is a relative term not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

(c) Claims 1-10 are grammatically incorrect at "for DNA immobilizing" and "for amplifying immobilizing DNA" in claim 1. It is suggested changing "DNA immobilizing" to "DNA immobilization" in lines 1-2 and in line 3, inserting "and" between "amplifying immobilizing" of claim 1.

(d) Claims 4 and 14 are confusing at "polar radial at terminal" because "terminal' has not been clearly described or defined in the specification and it is unclear where the claimed polar radical is located with respect to the substrate. See claim 12(a) for clarification.

(e) Claim 6-10 and 22-25 are indefinite because of improper claim format. It is suggested to amend the claims to recite for example,"wherein said polar radical is a carboxyl radical and said carboxyl radical is...".

(f) Claim 12 is confusing at DNA polymerize in step (c) because it is unclear what is meant by "DNA polymerize" or whether Applicant intended "DNA polymerase" as described in the specification at page 21.

(g) Claim 12 is confusing at amplifying DNA "for" a substrate "or" chip because it is unclear Applicant's intent or what is meant by "amplifying DNA "for" a substrate "or" chip. It is suggested to change "for" to "on".

(h) Claim 12 is indefinite because a relationship between substrate and "solution" in (c). It appears no step of "immobilizing" if that is intended. Step (c) is also confusing at "respect to" because it is unclear if DNA to be amplified is present.

(i) Claim 12 is indefinite at "TE" because "TE" has not been defined in the specification and abbreviations often have more than one meaning in the art. It is suggested inserting the full name of the agent.

(j) Claim 16 is not further limiting on claim 15 which states "DNA is immobilized on substrate".

(k) Claim 21 is rejected under 35 U.S.C. 112 second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. The omitted steps are actual steps of amplifying DNA on a solid substrate with the addition of a primer, four nucleotide bases, a polymerase and PCR reaction buffer as recited at page 21 of the specification. Additionally, making reference to the prior claim 5 is improper because claim 5 do not recite method steps of amplifying DNA but recites a substrate. Claim 1 which claim 5 is dependent from do not recite a method but only recite an intended use of the substrate. Clarification is required.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claim 1-5, 9-11, 13-16 and 25 are rejected under 35 U.S.C. 102(e) as being anticipated by Chrisey et al. (5,688,642, November 18, 1997). Regarding claims 1-5, 9-11, 13-16 and 25 disclose a solid state substrate or chip for immobilizing nucleic acid, wherein the substrate is diamond and is chemically modified (col. 1, lines 29-32 and col. 7, lines 21-26). Chrisey et al teach wherein the substrate has a polar radical at terminal wherein the polar radical is selected from the group consisting of an amino, hydroxyl or epoxy radical and wherein the polar radical is connected to the surface of said substrate or chip with a silane coupling agent (col. 7, lines 35-51) or through an ester linkage (col. 8, lines 9-12). Substantial thermal conductivity is an inherent feature of the diamond substrate as well known in the art. Therefore the claimed invention of claims 1-5, 9-11, 13-16 and 25 are anticipated by the reference of Chrisey et al.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 6-8 and 22-24 are rejected under 25 U.S.C. 103(a) as being unpatentable over Chrisey et al. in view of Adams et al. (5,641,658, June 1997) and further inn view of Weetall et al. (5,620,857, April 1997). Regarding claims 6-8 and 22-24, Chrisey et al. teach a substrate for DNA immobilization, said substrate have substantial thermal conductivity wherein the substrate is diamond and is chemically modified. Chrisey et al. also teach wherein the substrate has a polar radical at terminal wherein said polar radical is selected from the group consisting of hydroxyl, epoxyl or amino radical and wherein the polar radical is connected to the surface of the substrate with a silane coupling agent or through an ester linkage. Chrisey et al. further teach that the polar radical are used to promote immobilization of a nucleic acid to the surface of the substrate (col. 7, lines 34-35). The substrate of Chrisey et al. differ from the claimed invention in that the reference does not teach wherein a polar radical is a carboxyl radical which is connected to the surface of the substrate through an ester or amide linkage or wherein the carboxyl radical is connected to the surface of the substrate with a silane coupling agent, titanium coupling agent or aluminum coupling agent. However, substrates having a carboxyl radical at terminal are well known in the prior art. For example, Adams et al. teach a method for amplifying DNA comprising immobilizing DNA on a solid substrate wherein the substrate have thermal conductive characteristics and wherein said substrate is chemically modified at terminal with a carboxyl radical (See Abstract and col. 8, lines 19-29). Adams further

teach wherein the carboxyl radical is connected on the surface of the substrate through an amide linkage (see Example 1). Weetall et al. teach a solid substrate having a polar radical at terminal wherein said polar radical is selected from the group consisting of of epoxy, amine, carboxyl or hydroxyl radical and wherein the polar radical is attached to the surface of the substrate with a silane coupling agent (col. 5, example 1). In view of the foregoing, it would have been obvious to one or ordinary skill in the art at the time the invention was made to have been motivated to modify the substrate with a polar radical for the obvious benefit of promoting immobilization of a nucleic acid to the substrate as taught by Chrisey et al.

13. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. Regarding claim 12, Adams et al. teach a method for amplifying DNA for a substrate, comprising the steps of chemically modifying the substrate ro provide a polar radical on the surface, washing the substrate; dipping the substrate in a solution containing a primer with respect to amplifying target DNA, four kinds of nucleotide and DNA polymerase, holding the temperature of the solution at 94 degrees Celsius for one minute, holding the temperature of the solution at 55 degrees Celsius for about one minute; holding the temperature of said solution at 75 degrees Celsius for about five minutes and repeating the temperature steps (Example 1 and col. 12, lines 11-26). The method of Adams differs from the instant invention in that Adams does not teach wherein the solution is incubated at 95 degrees Celsius as the first temperature for one minute or wherein the second temperature is held at 45 degrees Celsius for about one and minute or wherein the third temperature is held at 74 degrees Celsius for about 2 minutes. However, as set forth by the court in *In re Aller*,

220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955), "where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation". The court has established that "a claim which falls within the broad scope of the references is held unpatentable thereover because, among other reasons, there is no evidence of the **criticality** of the claimed ranges (See *in re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA)). It would have been obvious to one of ordinary skill in the art at the time the invention was made optimize PCR of Adams et al. to shorter cycle times when smaller amount of product is desired.

Conclusion

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Cynthia Wilder whose telephone number is (703) 305-1680. The examiner can normally be reached on Tuesday through Friday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached at (703) 308-1152. The official fax phone number for the Group is (703) 308-4242. The unofficial fax number is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed the Group's receptionist whose telephone number is (703) 308-0196.

Cynthia B. Wilder

Cynthia B. Wilder, Ph.D.

June 4, 2001

S. Gromer